REMARKS

Claims 28, 29, 32-48 and 50-52 are currently pending in this application. Claims 28, 29, 32-48 and 50-52 are canceled and new claims 53-58 have been added. Support for the language contained in claim 53 is found on page 40, lines 15-18. Support for the language contained in claim 54 is found on page 3, line 12 *et seq.*, page 4, line 37 *et seq.* and page 44, line 4 *et seq.* Support for the language contained in claim 55 is found on page 3, lines 12-13 and on page 5, lines 12-13. Support for the language contained in claim 56 is found on page 44, lines 2-5. Support for the language contained in claim 57 is found on page 44, lines 5-9. Support for the language contained in claim 58 is found on page 10, lines 17-21 *et seq.* No new matter has been added. In view of these amendments and of the following remarks, Applicants believe that all the asserted rejections are in condition for withdrawal and all the claims are in condition for allowance.

Claims 28-29, 32-35, 47-48 and 50-52 stand rejected under 35 U.S.C. 112, second paragraph, for purported indefiniteness. The Examiner asserts that it is not clear as to exactly what constitutes "a" PLAG1 protein and in claims 32 and 42 "the PLAG1 fragment" lacks antecedent basis; that "amino acid" and "the sequence translated" lack antecedent basis; that it is not clear what is encompassed by the recitation "non-physiological proliferative capacity;" that in claims 34, 50 and 52 it is not clear what is meant by "corresponding" to the nucleic acid; and in claims 48 and 50 "the promoter region" lacks antecedent basis and it is not clear what sequence encompasses "the promoter region of a CTNNB1 gene."

Claims 28-29, 32-35, 47-48 and 50-52 stand rejected under 35 U.S.C. 112, first paragraph, for purported lack of written description with respect to new matter. The Examiner asserts that by using the recitation "'comprising' a sequence encoding 'a' PLAG1 protein," the claims encompass any sequence encoding "a" PLAG1 protein or fragment thereof, and any other flanking sequences for use in diagnosing cells having a non-physiological proliferative capacity, and that the specification does not provide such broad support for these claims.

Claims 28-29, 32-35, 47-48 and 50-52 stand rejected under 35 U.S.C. 112, first paragraph, for purported lack of written description. The Examiner asserts that the specification

fails to describe nucleic acids "comprising" sequences encoding "a" PLAG1 protein from SEQ ID NO: 116, or a fragment thereof, or at least one of the zinc fingers 1 to 7 represented by SEQ ID NOS: 117-123, or a sequence encoding the promoter region of a CTNNB1 gene, or at least one exon of the CTNNB1 gene because the claims are drawn to a large genus of possible sequences which are not contemplated or taught by the specification. The Examiner further asserts that the specification does not teach what constitutes or encompasses a "non-physiological proliferative capacity."

Claims 28-29, 32-35 and 47-48 (claim 49 previously has been cancelled) stand rejected under 35 U.S.C. 112, first paragraph, for purported lack of enablement. The Examiner asserts that while the specification is enabling for the cDNA sequence of the PLAG1 (SEQ ID NO: 116) protein, it does not provide enablement for sequences "comprising" any sequence encoding a PLAG1 protein or fragment thereof, any sequence comprising at least one of the zinc fingers 1 to 7, any sequence comprising a sequence encoding the promoter region of a CTNNB1 gene, and at least one exon of the CTNNB1 gene.

Claims 28 and 33-35 stand rejected under 35 U.S.C. 102(b) for purported anticipation by Tommerup et al. The Examiner asserts that Tommerup et al. teaches a cDNA encoding "a" PLAG1 protein and a fragment thereof that can be used to detect malignant disorders.

Claims 48 and 50-52 stand rejected under 35 U.S.C. 102(b) for purported anticipation by Nollet et al. The Examiner asserts that Nollet et al. disclose a sequence encoding the promoter region of a CTNNB1 gene and macromolecules comprising a nucleic acid comprising at least one exon of the CTNNB1 gene.

Claims 28-29, 32-48 and 50-52 have been cancelled and new claims 53-58 have been added that have clear support in the specification, enables one skilled in the art to practice the invention, and that more particularly point out and distinctly claim the subject matter of the invention. In particular, claims 53-58 are directed to an isolated nucleic acid sequence "consisting of" specific base pairs as depicted in Figure 4A or fragments thereof fused to a

nucleic acid sequence derived from a CTNNB1 protein that encodes a pleomorphic adenoma gene 1 (PLAG1) protein.

First, Applicants respectfully point out that "PLAG1 proteins" are clearly and explicitly described in the specification as follows:

> [A PLAG1 protein is] a protein with a deduced molecular weight of 56 kDa and a deduced pI of 8.56. Analysis of the open reading frame of [the] PLAG1 [protein] reveals seven zinc fingers in the amino-terminal region. The carboxy-terminal region is rich in serine residues. Furthermore, two potential nuclear localization signals are present (residues 22-25 and 29-32). Collectively, this suggests that the PLAG1 protein is a novel member of the large zinc finger gene family. (Page 4, lines 31-37)

Second, cancellation of claims 28-29, 32-48 and 50-52 renders moot the rejection of the claims based on lack of antecedent basis for "the amino acid," "the sequence translated," "the PLAG1 fragment" and "the promoter region." Additionally, the phrases "non-physiological proliferative capacity" and "the promoter region of the CTNNB1 gene" are no longer recited in the claims.

Third, the present invention as now claimed recites the preamble "consisting of" in place of "comprising," thus obviating the written description and enablement rejections. In particular, the isolated nucleic acid sequence of the present invention is now claimed as consisting of a specific number of base pairs of the PLAG1 gene located in specific exons of the gene which is fused to exon 1 of the CTNNB1 gene. With respect to the language "fragment of a nucleic acid," Applicants submit that one skilled in the art would know how to design fragments of a specific gene sequence in general, and the PLAG1 gene in particular in order to diagnose the presence of a particular tumor cell without undue or burdensome experimentation, as protocols for nucleic acid fragment isolation of a gene sequence based on a specific function of the nucleic acid fragment are well known and commonly employed in the art. Furthermore, with respect to new claims 54 and 55, Applicants agree with the Examiner that it is not necessary to disclose every species encompassed by a genus and, indeed, claims 56 and 57 recite particular species of the genera recited in claims 54 and 55.

Fourth, the present invention as now claimed inheres in an isolated nucleic acid sequence consisting of specific base pairs of PLAG1 located on exons 3 to 5 or fragments thereof fused to specific base pairs of a CTNNB1 gene located on exon 1, wherein the fused, i.e., hybrid, nucleic acid allows for the diagnosis of a cell as a tumor cell when it contains the hybrid nucleic acid sequence therein, and further wherein an isolated anti-sense nucleic acid sequence of the hybrid nucleic acid sequence or fragments thereof inhibit the expression of the hybrid nucleic acid sequence in tumor cells. Additionally, PLAG1 is located on chromosome 8, and the deduced amino acid sequence of the PLAG1 protein is not a Kruppel zinc finger protein because it does not contain the characteristic histidine/cysteine linker in between the zinc fingers.

In contrast to the above, Tommerup et al. disclose sixteen new zinc finger genes that belong to "Kruppel-family genes" and that are located on chromosomes 1-3, 5, 7, 11-12 and 19-20. Furthermore, Tommerup et al. disclose in result 4 of the SWISS-PROTEIN sequence search a match of less than 50% between zinc finger 2 of PLAG1 and zinc finger 7 of gene Z143. Thus, the very low homology with one zinc finger of PLAG1 disclosed by Tommerup et al. neither teaches nor suggests the existence of the isolated nucleic acid sequence of the present invention.

Fifth, the anticipation rejection in view of Nollet et al. is obviated because the present invention as now claimed no longer recites "a macromolecule comprising a nucleic acid in isolated form comprising a sequence encoding a region of a CTNNB1 gene."

Finally, Applicants respectfully submit that new claims 53-58 are proper for entry after a final rejection because the claims are more narrowly drawn to an isolated nucleic acid sequence consisting of specific base pairs as depicted in Figure 4A or fragments thereof fused to a nucleic acid sequence derived from a CTNNB1 protein, which encodes a pleomorphic adenoma gene 1 (PLAG1) protein and which allows for the diagnosis of a cell as a tumor cell when the tumor cell contains the hybrid nucleic acid sequence therein, and thus is the same invention which previously has been searched by the Examiner. Entry and allowance of new claims 53-58 are respectfully requested.

For all the foregoing reasons, new claims 53-58 are patentable over the cited prior art and in condition for allowance. Withdrawal of the asserted rejections and allowance of all pending claims 53-58 is respectfully requested.

Respectfully submitted,

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